

U.S.S.N. 09/714,602

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**AMENDMENT AND RESPONSE TO OFFICE ACTION****In the Claims**

1-2. (canceled)

3. (previously presented) The method according to Claim 57 further comprising after step (a),

removing auxotrophs from the plurality of mutant microorganisms.

Claims 4-56 (canceled)

57. (currently amended) A method for identifying a mutant microorganism having a reduced adaptation to a particular environment comprising the steps of

(a) providing a plurality of mutant microorganisms wherein each mutant microorganism contains an insertional mutation which incorporates a different marker sequence in a gene of the genome of the microorganism;

(b) introducing the plurality of mutants of step (a) into the said particular environment and allowing those microorganisms which are able to do so to grow in the said environment;

(c) retrieving microorganisms from the said environment or a selected part thereof; and

(d) selecting an individual mutant having a reduced capacity to proliferate in the particular environment by comparing marker sequences, if any, in the nucleic acid present in the retrieved microorganisms in step (c) to the different marker sequences referred to in step (a).

58. (previously presented) The method of Claim 57 for identifying a gene which allows a microorganism to adapt to a particular environment further comprising the step:

(e) identifying the gene which is mutated in the individual mutant having a reduced

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capacity to proliferate in the particular environment.

59. (previously presented) The method of Claim 58 for isolating a gene which allows a microorganism to adapt to a particular environment further comprising the step:

(f) isolating from a wild-type microorganism the corresponding wild-type gene.

60. (previously presented) The method of Claim 59 wherein the particular environment is a differentiated multicellular organism.

61. (previously presented) The method of Claim 60 wherein the multicellular organism is a plant.

62. (previously presented) The method of Claim 61 wherein the microorganism is a bacterium pathogenic to plants.

63. (previously presented) The method of Claim 61 wherein the microorganism is a fungus pathogenic to plants.

64. (previously presented) The method of Claim 60 wherein the multicellular organism is a non-human animal.

65. (previously presented) The method of Claim 64 wherein the animal is selected from the group consisting of a mouse, rat, rabbit, dog and monkey.

66. (previously presented) The method of Claim 65 wherein the animal is a mouse.

67. (previously presented) The method of Claim 64 wherein the microorganisms is a fungus pathogenic to animals.

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68. (previously presented) The method of Claim 67 wherein the fungus is selected from the group consisting of *Aspergillus* spp., *Cryptococcus neoformans* and *Histoplasma capsulatum*.

69. (previously presented) The method of Claim 64 wherein in step (b) the microorganisms are introduced orally, intravenously, intranasally, or intraperitoneally.

70. (previously presented) The method of Claim 69 wherein in step (c) the microorganisms are retrieved from the spleen.

71. (previously presented) The method of Claim 64 wherein the microorganism is a bacterium pathogenic to animals.

72. (previously presented) The method of Claim 71 wherein the bacterium is selected from the group consisting of *Bordetella pertussis*, *Campylobacter jejuni*, *Clostridium botulinum*, *Escherichia coli*, *Haemophilus decreyi*, *Haemophilus influenzae*, *Helicobacter pylori*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria* spp., *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pseudomonas* spp., *Salmonella* spp., *Shigella* spp., *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Vibrio* spp., and *Yersinia pestis*.

73. (previously presented) The method of Claim 60 wherein in step (c) the microorganisms are retrieved from the said environment at a site remote from the site of introduction in step (b).

74-75. (canceled).

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76. (previously presented) The method of Claim 57 wherein the microorganism is a bacterium.

77. (previously presented) The method of Claim 57 wherein the microorganism is a fungus.

78. (previously presented) The method of Claim 57 wherein in step (d) the comparison of any marker sequences in the nucleic acid of the mutants retrieved in step (c) to the marker sequences referred to in step (a) uses DNA amplification techniques and oligonucleotide primers.

Claims 79-86 (canceled)